

The following documents relate specifically to human chitinase and its potential physiological role under normal conditions and in disease states. Document C14 shows chitinase enzymatic activity in human leukocytes and in human serum, and speculates that it may contribute to host protection by cleaving chitin in the cell walls of fungal pathogens; the document does not report isolation of chitinase. Document C27 reports an elevation in chitotriosidase activity in the plasma of patients suffering from Gaucher disease; this document also does not report isolation of chitinase. Document C39 describes isolation of a chitinase (4-methylumbelliferyl-tetra-N-acetylchitotetraoside hydrolase) from human serum and rat liver.

Document C44 describes purification of human chitotriosidase from the spleen of a Gaucher disease patient, and also reports small portions of its amino acid sequence (22 amino terminal residues and 21 residues of a tryptic fragment). Document C6, which shares some co-authors with document C44, and which was published less than one year prior to the filing date of the present application, describes the cloning of a human macrophage cDNA with the same nucleotide sequence as that appearing in SEQ ID NO: 1 of this application (corresponding to clone MO-218). The cDNA sequence reported in document C6 differs from SEQ ID NO: 3 of the present application (corresponding to clone MO-13B) at position 330 of SEQ ID NO: 3, a nucleotide difference which results in an amino acid difference. Document B2, which was published after the filing date of the present application and therefore does not constitute prior art, describes the same cDNA clone (the sequence of Fig. 1) that is described in document C6, and a shorter cDNA clone (the sequence of Fig. 2) which is predicted to encode a 39kD protein. Document C60,

which was also published after the filing date of the present application and therefore does not constitute prior art, describes isoforms of human chitinases.

Document B3, which was published after the filing date of the present application and thus is not prior art, reports cloning of two chitotriosidase cDNAs (sequences set forth in Figs 1 and 2). The nucleotide sequence of Fig. 1 of B3 differs from SEQ ID NO: 1 of the present application at position 305, positions 476-481 (an insert relative to Fig. 1 of B3) and position 1234. The changes at positions 305 and 476-481 result in an amino acid difference as well. The nucleotide sequence of Fig. 1 of B3 differs from SEQ ID NO: 2 of the present application at positions 476-481 (an insert) and position 1234. The nucleotide sequence of Fig. 2 of B3 further differs from SEQ ID NOS: 1 and 2 at additional positions (see page 4, lines 16-24 of B3 describing the differences between the sequences of Figs. 1 and 2).

Document No.	Page no. of specification referencing document
B2	--
B3	--
C6	2, 12
C14	2
C27	10, 26
C39	2
C44	2, 12
C60	--

The following documents relate generally to chitinases from other, non-human sources, other chitinase-like polypeptides, and the potential role of chitinases and chitinase-like proteins under normal conditions and in disease states.

Document No.	Page no. of specification referencing document
B1	10
C3	--
C13	2, 11
C16	9
C17	11
C18	12
C19	12
C20	12
C21	2, 11
C23	1
C25	2, 11
C26	1
C29	2
C30	1
C32	1
C43	2
C47	9
C53	10
C55	--
C59	--

The following documents relate generally to experimental techniques.

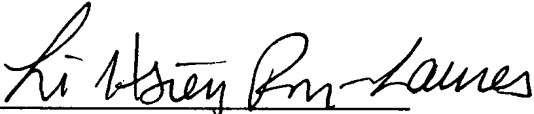
Document No.	Page no. of specification referencing document
C1	11
C2	29
C4	31
C5	17
C7	7
C8	30
C9	22
C10	22
C11	14
C12	22
C15	18
C22	29
C24	17
C28	33
C31	28
C33	16
C34	14
C35	34
C36	28
C37	28
C38	18
C40	32
C41	29
C42	17
C45	16
C46	30

Document No.	Page no. of specification referencing document
C48	18
C49	25
C50	17
C51	11
C52	28
C54	33
C56	--
C57	--
C58	--

Respectfully submitted,

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